BACKGROUND: For the treatment of a chronic disease like atopic dermatitis, sustained tolerability and efficacy of the applied medication are essential. OBJECTIVES: The present open-label, noncomparative study was conducted to obtain information on the long-term safety and efficacy of 0.1% tacrolimus ointment. METHODS: Patients aged 2 years or older with an affected body surface area of more than 5%, who previously participated in a clinical trial on tacrolimus ointment, were eligible for this study. The treatment area was defined by the investigator at study entry. Both children and adults applied continuously or intermittently 0.1% tacrolimus ointment twice daily during episodes of active disease plus an additional week after remission over a follow-up period of up to 4 years. RESULTS: The intent-to-treat population comprised 782 patients, with a median age of 22 years (range 2-72). Patients remained in the study for up to 4 years. Approximately half of the patients discontinued the study prematurely; the median follow-up was 1422 days. Median tacrolimus ointment use was 31.2 g during the first week; ointment use decreased during the first year and then remained stable for the remainder of the study. The median cumulative tacrolimus use was 271.5 g at month
6, 462.5 g at month 12, 739.9 g at month 24, 1029.3 g at month 36 and 1320.8 g at month 48.
Altogether 51.8% of patients discontinued the study prematurely; the main reasons were withdrawal of consent (13.3%), loss to follow-up (11.3%) and lack of efficacy (9.4%). Adverse events led to study discontinuation in 3.7% of the patients. The most frequent application site events were skin burning and pruritus. These events were most often reported in adult patients during the initial treatment period; prevalence decreased after the first week and remained at a low level throughout the study. Nonapplication site events occurred with stable incidences throughout the study period. In general, calculated daily hazard rates did not indicate an increased risk of adverse events with prolonged treatment. The total affected body surface area decreased substantially upon onset of treatment and efficacy of treatment was maintained until the end of the study with smaller but continuous improvements throughout the follow-up period. Overall, 75% of the patients and 76% of the investigators rated their satisfaction with the treatment as excellent, very good or good at the end of the study or at the time of premature discontinuation. CONCLUSIONS: The safety profile of intermittent or continuous long-term application of 0.1% tacrolimus ointment for up to 4 years was consistent with that which has been established from shorter studies and gave no reason for concern. In addition, 0.1% tacrolimus ointment demonstrated sustained efficacy as reflected by the expression of high satisfaction with treatment by both patients and investigators.